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Risk of developing cancer

Professor Alan White

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Professor White explained that he would move on from the starting point established by Professor Forman – that men are at greater risk of both developing and dying from the majority of cancers that might otherwise be assumed to affect both sexes equally. He would consider some possible explanations why this might be so. He would concentrate on some of the known causes of cancer and, in doing so, examine the evidence for factors that had particular relevance for men.

Professor White began by briefly examining the number of patients registered with cancer in different age groups. More men than women are registered for nearly all (non sex-specific) cancers at all ages. This confirms that the explanations are more complex than the assumption that more men than women die from cancer simply because men tend to delay seeking help. Professor White also drew attention to the incidence rates for cancer in children, where we see a broadly similar pattern to incidence rates in adults (although one that is perhaps not quite as clear cut – for example, kidney cancer is more common in girls than boys).

In thinking about causes of cancer, it is first important to recognise that there are two broad classes of cancer (although, as will be seen, there is overlap between them). The two classes are *germline cancers* (those that are attributable to inherited factors) and *somatic cancers* (those whose causes are acquired during the lifespan).

Germline

Various genetic mutations can be passed down through families making family

members of both sexes more susceptible to cancer (although the susceptibility may vary between men and women). Of particular interest in thinking specifically about men may be the association between some specific cancer risks and the known “vulnerability” of the XY (male) chromosome. Some authorities have also suggested that cancer cells may replicate more quickly in men. This latter point would not be addressed in the presentation but it was worth noting that it would probably bear further examination.

Professor White drew attention to some of the specific genetic mutations that have importance for men. BRCA2 is linked with breast cancer in women but men can have this mutation too. It is associated with the small risk of breast cancer in men but, more importantly for present purposes, with an increased risk of prostate cancer, stomach cancer and melanoma. There is a clear association between prostate cancer and the Y-chromosomal haplogroups, evidenced by the variation in rates between racial groups (for example, the incidence rate of prostate cancer in African-American males is double that of Caucasian men and ten times higher than Japanese men). Further evidence for inherited risk is the CHEK2 mutation, which doubles the risk of prostate cancer in general but quadruples the risk in men with family history of the disease. Likewise, standardised incidence ratios for testicular cancer suggest a familial association (risk increased 3.8-fold when a father had testicular cancer and 7.6-fold when a brother had the disease). Testicular cancer is further associated with increased familial risk of leukaemia, distal colon cancer, kidney cancer, melanoma, connective tissue tumours and lung cancer.

Somatic

It is believed that around 37% of cancers can be attributed to a group of specific lifestyle and environmental risk factors: smoking; alcohol use; low fruit and vegetable intake; overweight and obesity; physical inactivity; and urban air pollution (plus, in developing countries; unsafe sex, indoor smoke, and contaminated injections). Smoking is believed to be associated with 29% of cancer incidence in the UK – not just with lung cancer but with at least ten other cancers, including cancer of the oral and nasal cavities, oesophageal cancer and cancer of the bladder. As previously mentioned by Professor Forman, smoking is historically a particularly important risk factor for men. It is still the case that more men than women smoke in all age groups but rates of smoking in men are falling. As Professor Forman also pointed out, cancer risks associated with smoking may become more prevalent in women than men in decades to come.

Alcohol consumption is associated with a quantifiably increased risk of a number of cancers. One established explanation for this is that alcohol can cause damage to human cells. Animal studies suggest that alcohol consumption can also stimulate angiogenesis, unhelpfully increasing blood supply to existing cancers. Since excess alcohol consumption is more common in men than women, this adverse relationship between alcohol and cancer is more particularly a male problem. Excessive alcohol consumption is also associated with certain personal circumstances (e.g. being single, divorced or separated) which adds a complicating social dimension to the issue.

A diet high in fibre, fruit and vegetables has been shown to have a protective effect against cancer. Studies also suggest that some cancer risks are associated with particular foods (e.g. the association between eating red meat and cancers of the digestive system). Men and boys are markedly less likely than women and girls to eat the recommended five portions of fruit and vegetables daily. Numerous studies also have suggested a much lower interest in nutrition among men.

Ten percent of all deaths are believed to be associated with obesity. Several cancers are among the group of conditions whose risks are known to be exacerbated by obesity – including kidney cancer, cancer of the gall bladder, pancreatic cancer and prostate cancer. Among the known ways in which obesity contributes to the development of cancer are that obesity can cause acid reflux (a risk factor for oesophageal cancer); and hyperinsulinaemia (a predisposing factor for colon cancer).

Professor White commended the work of the Men's Health Forum which has, by pointing out that more men than women in the UK are overweight, consistently challenged the popular notion that weight is predominantly a "women's issue". In fact, two thirds of men are overweight compared with just over half of women – and it is estimated that by 2010 three quarters of UK men will be overweight. The differences between male and female physiology mean that men are more likely than women to gain fat around their abdomen. Abdominal fat is particularly associated with the secretion of numerous "fat toxins" at least one of which – leptin – is associated with increased cancer risk (in this case, prostate cancer).

Professor White had time only to offer pointers towards a number of other issues that potentially help explain some of the excess incidence of cancer in men:

- ▶ There is good evidence associating both excess exercise (perhaps as typically seen in young men interested in body-building) and too little exercise with increased risk of cancer. The numbers of men in sedentary occupations has grown very significantly in recent decades.

- ▶ Improvements in health and safety in the workplace have greatly reduced the likelihood of disease associated with known carcinogenic materials but it is probably true to say that men are much more likely than women to come into contact with a wide variety of potentially hazardous chemicals and materials including ultraviolet radiation; ionising radiation; pesticides; medical drugs; solvents; fibres; fine particles and dust; dioxins; polycyclic aromatic hydrocarbons (PAHs); metals; diesel exhaust particles; toxins from fungi; and vinyl chloride benzidine.

- ▶ Women are known to have both stronger humoral immune systems than men and stronger cellular immune systems. This means they have a more vigorous antibody reaction and greater resistance to viral and parasitic infections. Whether women also have more effective resistance to tumours might bear further investigation.

Finally, another factor that often attracts insufficient attention is the extent to which men are likely to develop and die from

particular cancers at younger ages than women. Colo-rectal cancer is a good example. Men tend to develop and die from this disease 5 – 10 years earlier than women. As already pointed out, there is a genetic component to colo-rectal cancer and known gene mutations are associated with it. Many of the known risk factors (obesity, poorer nutrition, higher alcohol intake and smoking) are seen to a greater extent in men. Diabetes, a disease which is known often to be diagnosed late in men is also linked to a higher risk of colo-rectal cancer. Do these factors potentially explain the difference in age of onset, as well as potentially explaining the difference in incidence rates? Certainly, no single factor can currently be seen as definitive, whether in relation to age or gender – this confirms the case that we need an all round approach to cancer prevention.



Professor Alan White

Professor Alan White: Conclusions

- ▶ **Men are at increased risk of many cancers.**
- ▶ **The causes of cancer are many and varied – both inherited and acquired.**
- ▶ **There are some known biological and lifestyle factors that seem to make men specifically vulnerable to developing cancer.**
- ▶ **But no systematic study of men's increased risk of cancer has yet been undertaken – indeed, no single specific paper on men and cancer is to be found in the literature at all.**